

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: **Bernstein and Warwick**

Serial No.: **10/539,140**

Group Art Unit: **1625**

Filed: **June 16, 2005**

Examiner: **David K. O'Dell**

Confirmation No.: **9263**

Title: **Piperidine Amine Compounds and Their Use**

Filed by EFS Web

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

RESPONSE UNDER 37 C.F.R. §1.111

In response to the Office Action dated August 19, 2008 in regard to the above-identified patent application, Applicants respectfully request reconsideration of the rejections therein.

Claims 2, 4-7, and 20 are pending in the present application.

I. The Claimed Invention Is Not Obvious

Claims 2, 4-7, and 20 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Stevenson et. al., J. Med. Chem., 1998, 41, 4623-4635 (hereinafter the "Stevenson reference"), in view of Bernstein et al., Bioorg. Med. Chem. Lett., 2001, 11, 2769-2773 (hereinafter the "Bernstein reference"). The Office asserts that one skilled in the art would have been motivated to modify compound 48 or 49 of the Stevenson reference by replacing the 2-methoxyphenyl group (from compound 48) or the 3,5-bis(trifluoromethyl)phenyl group (from compound 49) with the 3-cyanonaphthyl group of compound 4 of the Bernstein reference. Applicants traverse the rejection and respectfully request reconsideration.

When assessing whether or not a combination of references would have produced a claimed invention, one must consider the teaching of each reference as a whole without undue emphasis on those features that would support a finding of obviousness. *In re Wesslau*, 147 U.S.P.Q. 391 (C.C.P.A. 1965) (it is impermissible to pick and choose from any one reference only so much of it as will support a given position to the exclusion of other parts necessary to the full appreciation of what the references fairly suggest to one of ordinary skill in the art). Indeed, consideration of the Stevenson and Bernstein references as a whole for what they each fairly suggest, demonstrates that a person of ordinary skill seeking to combine them would not have produced any claimed invention.

In a first aspect, the Stevenson reference reports that when the $\text{-CH}_2\text{-O-CH}_2\text{-}$ linker of compound 12 is replaced with a $\text{-CH}_2\text{-NH-CH}_2\text{-}$ linker to form compound 49, the $\text{hNK}_1 \text{IC}_{50}$ increases from 0.95 ± 0.41 to 12.6 ± 8.8 . Thus, there is little, if any, motivation to use the $\text{-CH}_2\text{-NH-CH}_2\text{-}$ linker of compound 49. The Office asserts that “based on the experimental error involved these two values are ostensibly the same” (see, page 2 of the Office Action). Applicants disagree. Subtracting the entire “error” of 8.8 from the value of 12.6 results in a value of 3.8; adding the entire “error” of 0.41 to the value of 0.95 results in a value of 1.36; the value of 3.8 is almost three times as much as the value of 1.36. Thus, even taking into consideration the “error” in the two values, removing the $\text{-CH}_2\text{-O-CH}_2\text{-}$ linker from compound 12 of the Stevenson reference and replacing it with a $\text{-CH}_2\text{-NH-CH}_2\text{-}$ linker results in a compound with an almost 3-fold increase in $\text{hNK}_1 \text{IC}_{50}$. Thus, one skilled in the art examining the Stevenson reference as a whole would be led away from using the linker recited in the claims. Teachings in references that would have led one skilled in the art away from the invention are highly probative of nonobviousness. *Ashland Oil, Inc. v. Delta Resins & Refractories, Inc.*, 227 U.S.P.Q. 657 (Fed. Cir. 1985); and *Specialty Composites v. Cabot Corp.*, 6 U.S.P.Q.2d 1601 (Fed. Cir. 1988).

Even if one skilled in the art combined the Stevenson and Bernstein references in the manner suggested by the Office (and Applicants disagree with making such a combination), Applicants’ claimed invention still does not result. Claim 2 recites that “ R^4 and R^5 are, independently, selected from halogen, C_{1-4} alkoxy or halogenated C_{1-4} alkyl.” In contrast, the corresponding positions of compound 49 of the Stevenson reference and compound 4 of the

Bernstein reference are hydrogen. Thus, even if combined, the Stevenson and Bernstein references do not result in Applicants' claimed invention.

Thus, the claimed invention is not obvious in view of the combination of the Stevenson and Bernstein references. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. §103(a) be withdrawn.

II. Obviousness-Type Double Patenting

Claims 2, 4-7, and 20 are provisionally rejected under the doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-10 of co-pending Application No. 10/525,303 in view of the Stevenson reference, and further in view of Elliott et. al., Bioorganic & Med. Chem. Lett., 2002, 12, 1755-1758 (hereinafter, the "Elliott reference"). Applicants traverse this rejection and respectfully request reconsideration because the claimed subject matter is not an obvious variant of the subject matter recited in claims 1-10 of co-pending Application No. 10/525,303.

The Office asserts that the present obviousness-type double patenting rejection "is a one way obviousness test" (see, Office Action at page 3). The Office further asserts that "it would be obvious to replace CH₂ with C=O, to reduce the basicity, and the applicant is correct it would not be obvious to do the reverse, based on the teaching of Stevenson" (see, Office Action at page 3). The Office, however, appears to apply the one way obviousness test in the wrong direction.

An obviousness-type double patenting rejection is analogous to a failure to meet the nonobviousness requirement of 35 U.S.C. §103. *In re Braithwaite*, 154 U.S.P.Q. 29, 34 (C.C.P.A. 1967) and *In re Longi*, 225 U.S.P.Q. 645, 648 n.4 (Fed. Cir. 1985). Thus, under the law, the pivotal question in an obviousness-type double patenting analysis is: Does any claim in the application define merely an obvious variation of an invention disclosed and claimed in the patent? *In re Vogel*, 164 U.S.P.Q. 619 (C.C.P.A. 1970). If the answer to this question is no, there can be no double patenting. In making this analysis, then, the proper inquiry is as taught in *Graham v. John Deere Co.*, 383 U.S. 1 (1966). See, M.P.E.P. §804. Accordingly, the question to be answered in the present application is whether any claim in the present application defines merely an obvious variation of an invention disclosed and claimed in Applicants' co-pending

Application No. 10/525,303. Thus, the John Deere inquiry begins with the compounds disclosed in Applicants' co-pending Application No. 10/525,303, and any alleged motivation to modify those compounds by the reports in the Stevenson and Elliott references to arrive at Applicants' presently claimed compounds. According to the Office's own reasoning, that "it would be obvious to replace CH₂ with C=O, to reduce the basicity, and **the applicant is correct it would not be obvious to do the reverse**, based on the teaching of Stevenson" (see, Office Action at page 3), there is no motivation provided in the Stevenson reference for **removing** the carbonyl group from the compounds claimed in Applicants' co-pending Application No. 10/525,303, thus yielding them more basic (according to the Office), to arrive at Applicants' presently claimed invention. The Office appears to have applied the one-way test in the wrong direction. Accordingly, Applicants respectfully request that the provisional obviousness-type double patenting rejection be withdrawn.

III. Conclusion

In view of the foregoing, Applicants respectfully submit that the claims are in condition for allowance. An early notice of the same is earnestly solicited. The Office is invited to contact Applicants' undersigned representative at 610.640.7859 if there are any questions regarding Applicants' claimed invention.

Respectfully submitted,

/Paul K. Legaard, Reg.# 38534/
Paul K. Legaard, Ph.D.

Date: **18 November 2008**

Pepper Hamilton LLP
400 Berwyn Park
899 Cassatt Road
Berwyn, PA 19312-1183

Telephone: 610.640.7859
Facsimile: 267.430.7647